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Actigraphic Motor Activity in Mild Cognitive Impairment Patients Carrying Out Short Functional Activity Tasks: Comparison between Mild Cognitive Impairment with and without Depressive Symptoms

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Abstract.
Background: Individuals with mild cognitive impairment (MCI) may exhibit changes in motor activity in conducting their activities of daily living. Depression, one of the most frequent neuropsychiatric symptoms, might affect motor activity in MCI.
Objective: To assess motor activity in MCI subjects carrying out short functional activity tasks using ambulatory actigraphy. Secondly, we sought to investigate the influence of depressive symptoms on motor activity.
Methods: 20 MCI and 14 healthy subjects carried out a 30-minute standardized scenario while wearing a chest actigraph. The protocol consisted of directed activities (execution of motor tasks), semi-directed activities (execution of Instrumental Activities of Daily Living, IADL), and undirected 'free' activities. Several common assessment scales (GDS, MADRS, and NPI) were used to diagnose depression.
Results: MCI subjects had significantly reduced mean motor activity while carrying out directed and semi-directed activities, compared to healthy control subjects. No difference was found in motor activity between MCI subjects with or without depression.
Conclusion: Actigraphic measurement of motor activity during the evaluation of IADLs and motor tasks is a potential objective tool in detecting early changes in MCI. Depressive symptoms seem not to be associated with motor activity in MCI subjects.

Keywords: Actigraphy, depressive symptoms, mild cognitive impairment, motor activity

INTRODUCTION

Alzheimer's disease (AD) is the most common neurodegenerative disorder and major cause of mortality in old age [1, 2]. The progression of AD affects different domains of functioning, including cognitive, behavioral, and daily functioning [3]. Instrumental activities of daily living (IADLs) are complex activities required for independent living in a community [4]. Independent living requires the ability to perform activities such as managing money, taking medications, shopping, and housekeeping. IADLs are impaired in AD and

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subsequently lead to patients' loss of autonomy [5]. Patients with mild cognitive impairment (MCI) may show mild deficits in performance of complex activities of daily living [6]. Since assessment of IADLs is based on questionnaires, it is limited to some extent in reproducibility and objectivity. A French project launched under the name Sweet-HOME (2012) aimed to assess AD and MCI subjects' performance of the IADLs they would normally encounter in their home environment. The project used a video monitoring system coupled with several additional monitoring devices including actigraphy [7]. The assessment protocol consisted of three parts: (1) directed activities, (2) semi-directed activities, and (3) undirected ("free") activities. In the 'directed scenario', all participants' gait, balance, and mobility were assessed while they followed specific instructions. In the 'semi-directed scenario', memory and executive functions were evaluated while participants were instructed to follow instructions in a specific order. The 'free scenario' sought to provide information about the degree of interest and initiative that participants manifested on their own, without specific instructions. More details will be described in the methods section. The current study is an ancillary research to the 'Sweet-HOME project', specifically aimed at evaluating actigraphic measurements collected during IADLs' assessment, motor task performance, and a free scenario phase. Ambulatory actigraphy, consisting of a piezoelectric accelerometer designed to record body locomotor activity, has been previously used to evaluate various disorders including sleep-wake disorders, hyperactivity disorders, and dementia [8–10]. Recent studies have shown that daytime motor activity is reduced in AD patients compared to healthy controls [11–13]. Additionally, AD and MCI patients with apathy have been found to have reduced motor activity compared to those without apathy [13]. Neuropsychiatric disturbances are often observed in MCI and AD and frequently worsen during the progression of the disease [14, 15]. Alongside apathy, depression is one of the most common neuropsychiatric symptoms in AD with an estimated prevalence ranging from 20–50% [16, 17]. Depressive symptoms are associated with premature institutionalization and lower quality of life in early-stage AD patients [3, 18]. Furthermore, depression in patients with MCI increases the risk of developing AD [19]. These symptoms are also frequently observed in MCI and associated with greater brain atrophy and higher likelihood of progression to AD [20]. Hence, the presence of depressive symptoms in MCI might predict conversion from MCI to AD [21–23]. Furthermore, AD patients with depression have more difficulties in Activities of Daily Living (ADLs) compared to AD patients without depression [14]. A recent study by Vital et al. found that higher physical activity in AD patients is associated with fewer depressive symptoms [24]. The presence of depressive symptoms in MCI might be associated with motor activity changes during functional activity tasks.

The main aim of the present study was to evaluate levels of motor activity in MCI and healthy subjects carrying out a standardized scenario consisting of directed, semi-directed, and undirected activities, as described in the Sweet-HOME project. A second aim was to investigate the influence of depressive symptoms on mean motor activity (MMA) in MCI individuals carrying out the protocol. Our main hypotheses were: (i) MMA will be lower in MCI participants than in healthy control subjects; and (ii) MMA will be lower in MCI participants with depressive symptoms than in MCI participants without depressive symptoms and in healthy controls.

METHODS

Participants and clinical assessment

Participants aged 65 or older were recruited at the memory center in Nice located at the Geriatric department of the University Hospital. MCI diagnosis was conducted according to Petersen criteria [25]. Participants were excluded if they had a history of head trauma, loss of consciousness, aberrant motor behavior; scored higher than 0 on the Unified Parkinson's Disease Rating scale [26], and/or met criteria for major depression disorder according to DSM-IV [27]. However, participants with depressive symptoms were included in the study. The study was approved by a local ethics committee and all participants gave informed consent. General cognitive status was assessed using neuropsychological tests including: Mini-Mental State Examination (MMSE) [28], Frontal Assessment Battery (FAB) [29], and Instrumental Activities of Daily Living scale (IADL-E) [30]. Additionally, neuropsychiatric symptoms were assessed using the Neuropsychiatric Inventory scale (NPI) [31]. Since the prevalence of depressive symptoms in a group depends on the classification systems employed different classification scales were used: Montgomery–Åsberg Depression Rating Scale (MADRS) [32], Geriatric Depression Scale (GDS) [33], and NPI depression subscale. The NPI depression subscale was ultimately selected as the measure for depression, since other neuropsychiatric related

sub-symptoms such as anxiety and sleep disturbances are included in the MADRS and GDS [34, 35]. Participants were divided into two sub-groups based on their NPI depression scores. An NPI sub-score higher than three characterizes relevant clinical symptoms [36], thus individuals with a sub-score of 4 or higher on the NPI depression domain were included in the MCI subgroup with depressive symptoms. Depression was also separately diagnosed using GDS cutoff >10, MADRS cutoff >6, and NPI cutoff >0 to assess different diagnostic classification systems.

Ecological assessment of IADLs

In the Sweet-HOME project, impairment of daily functioning in MCI subjects was assessed using Information and Communication Technologies (ICT) such as a video monitoring system and actigraphy [7]. Participants were instructed to carry out a list of 10 activities in an observation room equipped with everyday objects: an armchair, a table, a tea preparation counter (equipped with the necessary material to prepare a cup of tea), a television set, a personal computer, and a library. Activity was also recorded with two monocular video cameras in the observation room. As mentioned earlier the protocol consisted of three different conditions. In the directed scenario, the examiner asked the participant to perform various physical exercises: a walking test, a balance exercise, a stand-up and go exercise, and a repeated rising from a chair to a stand test (10 min). In the semi-directed scenario participants had to carry out a set of daily living like activities such as making a phone call or preparing a pillbox in a specific order within a timeframe of 15 minutes. In the undirected activity scenario, participants were given 5 minutes free time in the observation room.

Actigraphic assessment

The Motionpod has been validated as a measurement of movement in several studies [37–39]. One of the objectives of our study was to validate the use the Motionpod Actigraph for the detection of motor activity levels in MCI and healthy subjects. The SVELTE project sought to develop an autonomous actimeter able to accurately record physical activity and associated energy expenditure with the MotionPod providing a highly accurate identification of physical activity patterns. Bonnet et al. [37] demonstrated the use of the MotionPod sensor for the detection of epileptic seizures. The MotionPod is an Inertial Measurement Unit that incorporates a 3-axis accelerometer, a 3-axis gyroscope, and a 3-axis magnetometer with a wireless interface. It cannot measure steps, but it indirectly measures energy expenditure using a dedicated algorithm.

During the course of the scenario, participants wore an actigraph (MotionPod®) attached to their chest using a dedicated band. Actigraph recording started from the beginning of the directed and semi-directed activities until the end of the ecological evaluation. The total recording time consisted of approximately 30 minutes, including directed, semi-directed, and free activities. Collected data consisted of integrated activity expressed in arbitrary units per second (Software Actigui 1.2.1, sampling frequency = 1 Hz (1 data/s)). In addition, each of the three activity scenarios was individually recorded on the actigraph.

Statistics analyses

Prior to analysis, data was verified for normality, potential outliers, and missing values. The distribution of the data was not normal, therefore group comparisons were made using non parametric Mann-Whitney U-Test. Categorical testing for gender and education was calculated using the chi-square test. Correlations were calculated using Spearman's rank-order correlation coefficient. All statistical analyses were computed using SPSS 14.0.

RESULTS

Characteristics of MCI subjects ($n = 20$, Age = 75.40 ± 6.69, MMSE = 25.95 ± 2.19) and healthy controls ($n = 14$, Age = 73.71 ± 6.57, MMSE = 28.07 ± 1.07) are presented in Table 1. The two groups did not significantly differ in age, gender, and education level. As expected, MCI and healthy controls had significantly different MMSE and FAB scores ($p < 0.05$). Furthermore, GDS and MADRS scores were significantly higher in MCI participants than in healthy controls ($p < 0.05$). No difference in IADL-E score was found between MCI and healthy controls. MCI participants, however, showed reduced MMA in the directed and semi-directed activity scenario ($p < 0.05$) compared to healthy controls, but not in the free and total activity scenario ($p = 0.122$ and $p = 0.07$, respectively). Subsequently, the MCI sample was divided into two subgroups; MCI with and without depressive symptoms, based on NPI score in the depression domain using a NPI-depression cut off score >3. Data of four participants were excluded because their NPI scores were not assessed. Table 2 represents characteristics for MCI subjects without depressive symptoms ($n = 10$,

Table 1
Characteristics and group comparisons for healthy controls and MCI subjects. Group comparisons were made using Mann-Whitney U test ($p < 0.05$) and chi-square ($p < 0.05$) for categorical testing. Categorical testing for education was analyzed with Pearson chi-square. Data shown as mean ± SD

	Controls ($n = 14$)	MCI ($n = 20$)	p
Gender (female/male)	8/6.	8/12.	0.49
Age (years)	73.71 ± 6.57	75.40 ± 6.69	0.46
Education category			0.59
Primary	3/14	5/20	
Secondary	5/14	9/20	
College	1/14	3/20	
University	5/14	3/20	
Mini-mental state examination	28.07 ± 1.07	25.95 ± 2.19	**0.01**
Frontal assessment battery	15.71 ± 1.54	13.95 ± 2.19	**0.03**
Instrumental activities of daily living	9.64 ± 1.15	9.47 ± 1.89	0.65
Geriatric depression scale	6.00 ± 6.3	10.75 ± 5.73	**0.02**
MADRS	2.86 ± 2.66	6.75 ± 6.34	**0.02**
NPI delusion	*	0.00 ± 0.00	–
NPI hallucination	*	0.00 ± 0.00	–
NPI agitation	*	0.93 ± 3.00	–
NPI depression	*	2.17 ± 2.43	–
NPI anxiety	*	1.50 ± 2.25	–
NPI euphoria	*	0.00 ± 0.00	–
NPI apathy	*	1.50 ± 3.22	–
NPI disinhibition	*	0.57 ± 2.00	–
NPI aberrant motor	*	0.00 ± 0.00	–
NPI sleep	*	1.75 ± 2.38	–
NPI appetite	*	0.50 ± 1.37	–
NPI total	*	10.32 ± 7.56	–
MMA total (30 min)	0.050 ± 0.01	0.045 ± 0.01	0.074
MMA directed activities (10 min)	0.065 ± 0.02	0.054 ± 0.01	**0.033**
MMA semi-directed activities (15 min)	0.047 ± 0.01	0.040 ± 0.01	**0.022**
MMA free activities (5 min)	0.038 ± 0.01	0.028 ± 0.01	0.122

*NPI was not assessed in the control population. Bold characters represent significant p-values <0.05. MADRS, Montgomery-Åsberg Depression Rating Scale; MMA, mean motor activity; NPI, Neuropsychiatric Inventory.

Age = 76.60 ± 6.72, MMSE = 25.80 ± 2.44) and MCI with depressive symptoms ($n = 6$, Age = 77.17 ± 7.90, MMSE = 25.5 ± 2.26). No significant difference was found in age, gender, education level, MMSE, FAB, and IADLs scores, between MCI with and MCI without depressive symptoms. The two subgroups were equivalent on all NPI-scored domains expect depression and total NPI score. MCI subjects with depressive symptoms had significantly higher MADRS score ($p < 0.05$), whereas the difference in GDS was not statistically significant ($p = 0.06$). In all three scenarios, MMA did not significantly differ between the two subgroups. Results were similar when defining depression using GDS (cutoff >10), MADRS (cutoff >6), or NPI >0 cut-off score.

DISCUSSION

The present study found that MCI participants showed significantly reduced MMA while carrying out directed and semi-directed activities, compared to healthy controls. Previous actigraphic studies have found lower levels of motor activity in dementia compared to healthy controls, and can discriminate between MCI and AD patients with and without apathy [11–13]. However, one study specifically investigated motor activity in MCI subjects over a 5-day non-directed actigraphic assessment period [13] and found reduced motor activity in MCI subjects with apathy but not in MCI subjects without apathy. In the present study, we did not find differences in motor activity during the undirected free scenario. Hence, our study is the first one demonstrating that MCI subjects have lower motor activity level compared to healthy controls, while carrying out IADLs and motor tasks in a clinical setting. Even though, it has been previously shown that depression is often associated with decreased motor activity [11–13, 40–42], we did not find any association between depressive symptoms in MCI subjects and motor activity. In the present study, depressive symptoms, as measured by GDS and MADRS scores, were more frequently observed in MCI subjects than in healthy controls. The prevalence of depressive symptoms depends on the classification systems employed [43]. A sub-score above 0 has previously been used to define mild depressive symptoms in the NPI [20]. However, in this study, we used an NPI cut-off score greater than three as the main diagnostic test for indicating clinically significant depressive symptoms [36]. Additionally, we found no association between motor activity and depressive symptoms when defining depression in MCI using the GDS, MADRS, and NPI cut-off score above 0. No significant correlation was found between depression scale scores and motor activity in MCI and healthy controls. The prevalence of depressive symptoms varied across depression scales used for this study, with the highest prevalence rate (68.7%) when we used the NPI >0 cutoff score, and 37.5% when we used both MADRS and NPI >3; group assignment was different however for six participants. Overall, this study, in agreement with previous studies reporting high variability in the prevalence of depressive symptoms in MCI [17], shows that prevalence of depressive symptoms in MCI depends on the diagnostic criteria used. This might be related to methodological differences, such as different diagnostic criteria, variability in cut-off scores, and environmental factors. Hence, our study

Table 2
Characteristics and group comparisons for MCI with and without depressive symptoms. Groups were analyzed with Mann-Whitney U test ($p < 0.05$) and chi-square ($p < 0.05$) for categorical testing. Categorical testing for education was analyzed with Pearson chi-square test. Data shown as mean ± SD

	MCI without depressive symptoms ($n = 10$)	MCI with depressive symptoms ($n = 6$)	p
Gender (female/male)	5/5	3/3	1.00
Age (years)	77.6 ± 6.72	77.17 ± 7.90	0.30
Education category			0.62
Primary	2/10	3/6	
Secondary	4/10	2/6	
College	2/10	0/6	
University	2/10	1/6	
Mini-mental state examination	25.8 ± 2.44	25.5 ± 2.26	0.58
Frontal assessment battery	14.00 ± 2.62	13.67 ± 1.97	0.87
Instrumental activities of daily living	9.50 ± 2.12	8.80 ± 1.92	0.71
Geriatric depression scale	8.70 ± 5.96	13.50 ± 3.67	0.06
MADRS	5.00 ± 2.16	7.00 ± 3.58	**0.03**
NPI delusion	0.00 ± 0.00	0.00 ± 0.00	1.00
NPI hallucination	0.00 ± 0.00	0.00 ± 0.00	1.00
NPI agitation	1.20 ± 3.79	0.50 ± 8.36	0.34
NPI depression	0.70 ± 8.23	5.00 ± 1.67	**0.00**
NPI anxiety	0.90 ± 1.29	2.50 ± 3.20	0.48
NPI euphoria	0.00 ± 0.00	0.00 ± 0.00	1.00
NPI apathy	0.80 ± 1.69	2.67 ± 4.84	0.47
NPI disinhibition	0.90 ± 2.51	0.00 ± 0.00	0.26
NPI irritability	0.70 ± 1.89	2.17 ± 3.00	0.07
NPI aberrant motor	0.00 ± 0.00	0.00 ± 0.00	1.00
NPI sleep	1.60 ± 1.78	2.00 ± 3.35	0.90
NPI appetite	0.40 ± 1.26	0.67 ± 1.63	0.70
NPI total	7.20 ± 7.77	15.00 ± 3.33	**0.02**
MMA total (30 min)	0.047 ± 0.011	0.039 ± 0.004	0.13
MMA directed activities (10 min)	0.055 ± 0.010	0.053 ± 0.012	1.00
MMA semi-directed activities (15 min)	0.040 ± 0.004	0.035 ± 0.004	0.12
MMA free activities (5 min)	0.030 ± 0.011	0.039 ± 0.040	0.44

Bold characters represent significant p-values <0.05. MADRS, Montgomery-Åsberg Depression Rating Scale; MMA, mean motor activity; NPI, Neuropsychiatric Inventory.

further underlines the difficulties in diagnosing depressive symptoms in MCI patients. Since no differences between motor activity among MCI subjects with or without depression were found even when using different scales, it may be that depression, contrary to apathy, is not associated with motor activity in MCI patients. Therefore, actigraphy could be a more effective tool for objectively assessing apathy rather than depression in subjects with MCI. Nevertheless, our failure to find an association between depressive symptoms and motor activity in MCI subjects could be due to the limited power of our study.

The main limitation of this study is the small sample size. A second limitation is that the MCI subjects, in our study, had low NPI sub-scores for agitation, depression, anxiety, apathy, irritability, and disinhibtion, all of which could potentially influence levels of motor activity using actigraphy. Apathy, although known to influence actigraphic analyses, was not frequent in our sample [12, 13]. According to the diagnostic criteria for apathy proposed by Robert at al. only 3 out of 20 MCI subjects were diagnosed with apathy [44].

Impairment in motor function is a common manifestation in AD [45, 46]. Changes in subcortical white matter, hippocampus, and the dopaminergic system have been implicated in motor impairment found in AD [47, 48]. It is known that motor function and motor activity levels are related, however, this phenomenon remains largely unstudied. In a recent study, James et al. assessed motor function by measuring muscle strength and a broad range of motor performance such as walking and balance. Further, physical activity was measured by a wrist-worn actigraph [49]. The study showed that lower levels of daily physical activity measured by actigrahy were associated with lower levels of motor function. Additionally, motor activity and motor function were both lower in demented participants. Interestingly, we found reduced motor activity in MCI subjects in the directed and semi-directed scenario, which involved different components of motor

function. No difference in motor activity between MCI and healthy controls was observed during the undirected scenario. This can be explained by the fact that during this scenario almost all participants in both groups passively sat on the couch for a period of 5 minutes. Hence, it may be that motor activity in MCI results from impaired motor function. Nevertheless, the same neurobiological mechanism could underlie both impaired motor function and motor activity. Further research is needed to understand the relationship between motor function and motor activity levels.

This study presents some major novel findings: (1) MCI patients carrying out directed and semi-directed activities have lower motor activity compared to healthy controls; and (2) actigraphic measurement of motor activity during the evaluation of IADLs and motor tasks is a potential objective tool in detecting early changes in MCI, with higher accuracy and sensitivity than the IADL-E, because no significant difference was found in the IADL-E. This finding could have a significant impact on diagnosis and assessment of MCI in clinical practice. Assessments of IALDs and motor performance can easily be conducted in clinical practice. Clinicians could employ this assessment procedure during a regular consultation to improve diagnosis and detect early changes in MCI. Future studies could be carried out in participants' home environments combining actigraphy with other ICTs such as movement sensors, imaging, and video processing. This approach could aid in detecting early changes in motor performance and activity in cognitively impaired patients.

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